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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/523,276

09/19/2005

Danilo Giribone

18614 (PCT27405A)

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EXAMINER

KOSACK, JOSEPH R

ART UNIT

PAPER NUMBER

1626

MAIL DATE

DELIVERY MODE

11/14/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/523,276	Applicant(s) GIRIBONE ET AL.	
	Examiner Joseph R. Kosack	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 August 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-6 are pending in the instant application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 6, 2008 has been entered.

Previous Claim Rejections - 35 USC § 102

Claims 1-4 were previously rejected under 35 U.S.C. 102(b) as anticipated by Tang et al. (USPN 5,834,504).

Applicant has asserted that the amendment to claim 1 to revise the definition of m to exclude 0 removes the anticipated subject matter. Applicant is correct in the case of claims 1, 2, and 4, however claim 3 still contains an anticipated species and the rejection is maintained for claim 3. The rejection is withdrawn for claims 1, 2, and 4.

Previous Claim Rejections - 35 USC § 103

Claims 1-5 were previously rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al. (USPN 5,834,504) in view of Plieninger et al. (*Liebigs Ann. Chem.* 1972, 195-201).

Applicant has asserted that the amendment to claim 1 to revise the definition of m to exclude 0 removes the anticipated subject matter. Applicant is correct in the case

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of claims 1, 2, 4, and 5, however claim 3 still contains an anticipated species and the rejection is maintained for claim 3. The rejection is withdrawn for claims 1, 2, 4, and 5.

Claim 6 was previously rejected under 35 U.S.C. 103(a) as being unpatentable over Plieninger et al. (*Liebigs Ann. Chem.* 1972, 195-201).

Applicant has traversed the rejection on the grounds that one of skill in the art would not be motivated to change a hydrogen group to a methyl group and that there is no disclosure in Plieninger et al. to motivated the person of ordinary skill. Applicant has also cited the decisions in *KSR v. Teleflex* and *Takeda v. Alphapharma* in support of the traversal.

The Examiner must respectfully disagree. Firstly, the court decisions cited by the Applicant are not commensurate in scope with the instant fact pattern. Secondly, the decision in *KSR* specifically states that motivation may be found not only in the prior art that is cited, but also in other forums such as market pressures, common sense, equivalents, etc... As the courts have already ruled that hydrogen and methyl are obvious variants in the absence of some form of secondary considerations, the motivation is present and the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

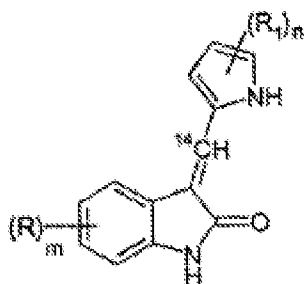
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claim 3 rejected under 35 U.S.C. 102(b) as anticipated by Tang et al. (USPN 5,834,504).

The instant application is drawn to compounds of formula I:

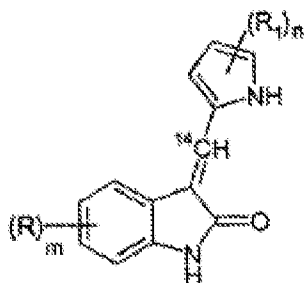


with substitutions as defined. Included is the species 3-[(3,5-dimethyl-1H-pyrrol-2-yl)[^{14}C]methylene-1,3-dihydro-2H-indol-2-one.

Tang et al. teach the compound 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene-1,3-dihydro-2H-indol-2-one. This reads on the claims because ^{14}C is within the natural abundance of carbon atoms and therefore the compound is inherently present in Tang et al.'s synthesis. See column 22, lines 42-49.

Claims 1, 2, and 4 rejected under 35 U.S.C. 102(b) as anticipated by Tang et al. (WO 96/40116).

The instant application is drawn to compounds of formula I:



with substitutions as defined as well as a method of making by

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reacting an optionally substituted pyrrolinecarboxaldehyde with an oxindole in basic conditions.

Tang et al. teach the compound 5-chloro-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene-1,3-dihydro-2H-indol-2-one along with the method of making by reacting the oxindole with optionally substituted pyrrolinecarboxaldehyde in piperidine. This reads on the claims because ^{14}C is within the natural abundance of carbon atoms and therefore the compound is inherently present in Tang et al.'s synthesis. See column 22, lines 42-49.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

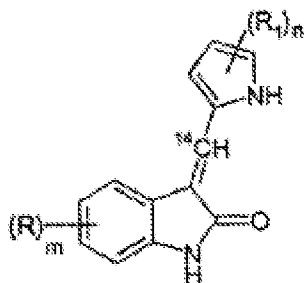
The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 3 rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al. (USPN 5,834,504) in view of Plieninger et al. (*Liebigs Ann. Chem.* 1972, 195-201).

The instant application is drawn to compounds of formula I:



with substitutions as defined and a method of making by reacting an optionally substituted pyrrolinecarboxaldehyde with an oxindole in basic conditions, specifically pyrrolidine. Included is the species 3-[(3,5-dimethyl-1H-pyrrol-2-yl)[¹⁴C]methylene-1,3-dihydro-2H-indol-2-one.

Determination of the scope and content of the prior art (MPEP §2141.01)

Tang et al. teach the compound 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene-1,3-dihydro-2H-indol-2-one along with the method of making by reacting the oxindole with

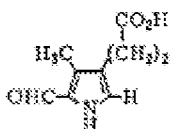
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optionally substituted pyrrolinecarboxaldehyde in piperidine. See column 22, lines 42-49.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Tang et al. do not teach that ^{14}C is present in the methylene group in more than the natural abundance, nor that the synthesis is done in pyrrolidine.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)



Plieninger et al. teach in which the carbon of the aldehyde group is ^{14}C . See page 196, compound 5 and page 198, second full paragraph. One of skill in the art would be able to make the switch from piperidine to pyrrolidine as the base for reaction as they are both cyclic nitrogenous bases. Additionally, one of skill in the art routinely uses radioisotopes for studies within the body for absorption, distribution, metabolism, and excretion studies.

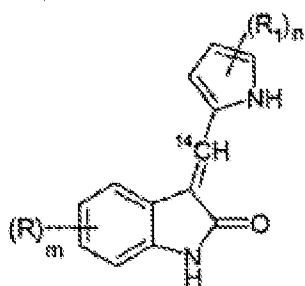
Therefore, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention was made to follow the synthetic scheme of Tang et al. with the ^{14}C replacement of Plieninger et al. using pyrrolidine instead of piperidine to make the claimed invention with a reasonable expectation of success. The motivation to do so is that radiolabeled compounds can be easily analyzed by mass spectroscopy in order to determine various aspects of the body, such as how much unnatural testosterone is within a human's system.

Thus, the claimed invention as a whole was *prima facie* obviousness over the combined teachings of the prior art.

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Claim 1, 2, 4, and 5 rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al. (WO 96/40116) in view of Plieninger et al. (*Liebigs Ann. Chem.* 1972, 195-201).

The instant application is drawn to compounds of formula I:



with substitutions as defined and a method of making by reacting an optionally substituted pyrrolinecarboxaldehyde with an oxindole in basic conditions, specifically pyrrolidine.

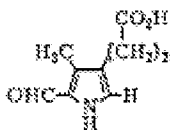
Determination of the scope and content of the prior art (MPEP §2141.01)

Tang et al. teach the compound 5-chloro-3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-2H-indol-2-one along with the method of making by reacting the oxindole with optionally substituted pyrrolinecarboxaldehyde in piperidine. See column 22, lines 42-49.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Tang et al. do not teach that ^{14}C is present in the methylene group in more than the natural abundance, nor that the synthesis is done in pyrrolidine.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)



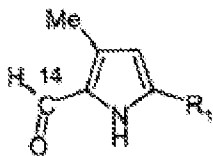
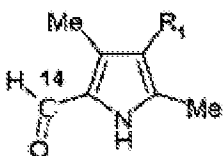
Plieninger et al. teach in which the carbon of the aldehyde group is ^{14}C . See page 196, compound 5 and page 198, second full paragraph. One of skill in the art would be able to make the switch from piperidine to pyrrolidine as the base for reaction as they are both cyclic nitrogenous bases. Additionally, one of skill in the art routinely uses radioisotopes for studies within the body for absorption, distribution, metabolism, and excretion studies.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention was made to follow the synthetic scheme of Tang et al. with the ^{14}C replacement of Plieninger et al. using pyrrolidine instead of piperidine to make the claimed invention with a reasonable expectation of success. The motivation to do so is that radiolabeled compounds can be easily analyzed by mass spectroscopy in order to determine various aspects of the body, such as how much unnatural testosterone is within a human's system.

Thus, the claimed invention as a whole was *prima facie* obviousness over the combined teachings of the prior art.

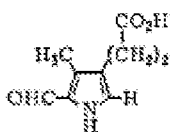
Claim 6 rejected under 35 U.S.C. 103(a) as being unpatentable over Plieninger et al. (*Liebigs Ann. Chem.* 1972, 195-201).

The instant application is drawn to compounds of the formulae



with substitutions as defined.

Determination of the scope and content of the prior art (MPEP §2141.01)



Plieninger et al. teach

in which the carbon of the aldehyde group is

¹⁴C. See page 196, compound 5 and page 198, second full paragraph.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Plieninger et al. do not teach a methyl group in the 5-position of the pyrrolidine.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

It is known that compounds having similar structures have similar effects, especially when the difference is a hydrogen over a methyl group, which also provides the motivation and the reasonable expectation of success. See the decision of In re Wood, Whittaker, Stirling, and Ohta (199 USPQ 137).

Thus, the claimed invention as a whole was *prima facie* obviousness over the combined teachings of the prior art.

Conclusion

Claims 1-6 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph R. Kosack whose telephone number is (571)272-5575. The examiner can normally be reached on M-Th 6:30-5:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Joseph R Kosack/
Examiner, Art Unit 1626

/REI-TSANG SHIAO /
Primary Examiner, Art Unit 1626